FORM PTO-1390
(Rev 10-9-94)

U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office
Docket No. 229752001000

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. § 371

09/44667

U.S. APPLICATION NO. (If known, see 37 C.F.R. § 1.5): Unassigne

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/AU 98/00519	July 6, 1998	July 7, 1997

TITLE OF INVENTION: SHAPED PRODUCTS OR STRUCTURES FOR MEDICAL OR RELATED PURPOSES

APPLICANT(S) FOR DO/EO/US: VAGO, Razo

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. § 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. § 371.
3. ☒ This express request to begin national examination procedures (35 U.S.C. § 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. § 371(b) and PCT Articles 22 and 39(1).
4. ☒ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. ☒ A copy of the International Application as filed (35 U.S.C. § 371(c)(2))
   a. ☒ is transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☒ has been transmitted by the International Bureau.
   c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US)
6. ☒ A translation of the International Application into English (35 U.S.C. § 371(c)(2)).
7. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. § 371(c)(3))
   a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☐ have been transmitted by the International Bureau.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ☒ have not been made and will not be made.
8. ☐ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. § 371(c)(3)).
9. ☐ An oath or declaration of the inventor(s) (35 U.S.C. § 371(c)(4)).
10. ☐ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. § 371(c)(5)).

Items 11. to 16. below concern document(s) or information included:

11. ☐ An Information Disclosure Statement under 37 C.F.R. §§ 1.97 and 1.98.
12. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 C.F.R. §§ 3.28 and 3.31 is included.
13. ☐ A FIRST preliminary amendment.
    ☐ A SECOND or SUBSEQUENT preliminary amendment.
14. ☐ A substitute specification.
15. ☐ A change of power of attorney and/or address letter.
16. ☒ Other items or information: various PCT documents, including PCT request, PCT/IB/306, PCT/IPEA/409, Interr Search Report; return receipt postcard.

CERTIFICATE OF HAND DELIVERY

I hereby certify that this correspondence is being hand-carried to : AssistanCommissioner for Patents, Washington, D.C. 20231, on December 2

Jinrong Li

dc-187710

514 Rec'd PCT/PTO 23 DEC 1999

U.S. APPLICATION NO. (If known, see 37 C.F.R. § 1.5) 09/446827 Unassigned	INTERNATIONAL APPLICATION NO. PCT/AU98/00519	DOCKET NUMBER: 229752001000

17. ☒ The following fees are submitted:

BASIC NATIONAL FEE (37 C.F.R. §§ 1.492(a)(1)-(5)):

Search Report has been prepared by the EPO or JPO $840.00

International preliminary examination fee paid to (USPTO (37 C.F.R. § 1.482) $670.00

No international preliminary examination fee paid to USPTO (37 C.F.R. § 1.482) but international search fee paid to USPTO (37 C.F.R. § 1.445(a)(2)) $760.00

Neither international preliminary examination fee (37 C.F.R. § 1.482) nor international search fee (37 C.F.R. § 1.445(a)(2)) paid to USPTO $970.00

International preliminary examination fee paid to USPTO (37 C.F.R. § 1.482) and all claims satisfied provisions of PCT Article 33(2)-(4) $96.00

CALCULATIONS PTO USE ONLY

			ENTER APPROPRIATE BASIC FEE AMOUNT =	$970.00	
Surcharge of **$130.00** for furnishing the oath or declaration later than ☐ 20 ☒ 30 months from the earliest claimed priority date (37 C.F.R. § 1.492(e)).				$130.00	
CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE	$0.00	
Total claims	21 - 20 =	1	1x $18.00	$18.00	
Independent claims	1 - 3 =		x $78.00	$.00	
MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ $260.00	$260.00	
			TOTAL OF ABOVE CALCULATIONS =	$1,378.00	
Reduction by ½ for filing by small entity, if applicable. Verified Small Entity Statement must also be filed (Note 37 C.F.R. §§ 1.9, 1.27, 1.28)				$0.00	
			SUBTOTAL =	$1,378.00	
Processing fee of **$130.00** for furnishing the English translation later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 C.F.R. § 1.492(f)).			+	$0.00	
			TOTAL NATIONAL FEE =	$1,378.00	
Fee for recording the enclosed assignment (37 C.F.R. § 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 C.F.R. §§ 3.28, 3.31). **$40.00 per property**			+	$0.00	
			TOTAL FEES ENCLOSED =	$1,378.00	
				Amount to be refunded:	**$689.00**
				charged:	**$**

a. ☒ A check in the amount of $ 1,378.00 to cover the above fees is enclosed.

b. ☒ The Assistant Commissioner is hereby authorized to charge any additional fees that may be required, or credit any overpayment to **Deposit Account No. 03-1952**.

NOTE: Where an appropriate time limit under 37 C.F.R. § 1.494 or 1.495 has not been met, a petition to revive (37 C.F.R. § 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

Barry E. Bretschneider
Morrison & Foerster LLP
2000 Pennsylvania Avenue, N.W.
Washington, D.C. 20006-1888

SIGNATURE

Barry E. Bretschneider
Registration No. (28,055)

dc-187710

09/446629
Rec'd PCT/PTO 23 MAR 2000

Applicant or Patentee: Razi VAGO
Serial or Patent No.: _____
Filed or Issued: _____
For: "Shaped products or structures for medical or related purposes"

Attorney's Docket No.: _____

VERIFIED STATEMENT (DECLARATION) CLAIMING SMALL ENTITY STATUS (37 CFR 1.9(f) and 1.27(b)) - INDEPENDENT INVENTOR

As a below named inventor, I hereby declare that I qualify as an independent inventor as defined in 37 CFR 1.9(c) for purposes of paying reduced fees under section 41(a) and (b) of Title 35, United States Code, to the Patent and Trademark Office with regard to the invention entitled "Shapped products or structures for medical or related purposes" described in

[ ] the specification filed herewith
[X] application serial no. _____, filed _____
[ ] patent no. _____, issued _____

I have not assigned, granted, conveyed or licensed and am under no obligation under contract or law to assign, grant, convey or license, any rights in the invention to any person who could not be classified as an independent inventor under 37 CFR 1.9(c) if that person had made the invention, or to any concern which would not qualify as a small business concern under 37 CFR 1.9(d) or a nonprofit organization under 37 CFR 1.9(e).

Each person, concern or organization to which I have assigned, granted, conveyed, or licensed or am under an obligation under contract or law to assign, grant, convey, or license any rights in the invention is listed below:

[ ] no such person, concern, or organization
[X] persons, concerns or organizations listed below*

*NOTE: Separate verified statements are required from each named person, concern or organization having rights to the invention averring to their status as small entities. (37 CFR 1.27)

FULL NAME AUSTRALIAN INSTITUTE OF MARINE SCIENCE
ADDRESS Cape Cleveland Road, Cape Ferguson, Townsville,Queensland,4810,Australi
[ ] INDIVIDUAL [ ] SMALL BUSINESS CONCERN [X] NONPROFIT ORGANIZATION

FULL NAME _____
ADDRESS _____
[ ] INDIVIDUAL [ ] SMALL BUSINESS CONCERN [ ] NONPROFIT ORGANIZATION

FULL NAME _____
ADDRESS _____
[ ] INDIVIDUAL [ ] SMALL BUSINESS CONCERN [ ] NONPROFIT ORGANIZATION

I acknowledge the duty to file, in this application or patent, notification of any change in status resulting in loss of entitlement to small entity status prior to paying, or at the time of paying, the earliest of the issue fee or any maintenance fee due after the date on which status as a small entity is no longer appropriate. (37 CFR 1.28(b))

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

NAME OF INVENTOR	NAME OF INVENTOR	NAME OF INVENTOR
Razi VAGO		
Signature of Inventor	Signature of Inventor	Signature of Inventor
27/02/2000		
Date	Date	Date

23 MAR 2000

Applicant or Patentee: Razi VAGO 09/446629 Attorney's
Serial or Patent No.: Docket No:
Filed or Issued:
For: "Shaped products or structures for medical or related purposes"

VERIFIED STATEMENT (DECLARATION) CLAIMING SMALL ENTITY STATUS (37 CFR 1.9(f) and 1.27(d)) - NONPROFIT ORGANIZATION

I hereby declare that I am an official empowered to act on behalf of the nonprofit organization identified below:

NAME OF ORGANIZATION AUSTRALIAN INSTITUTE OF MARINE SCIENCE
ADDRESS OF ORGANIZATION Cape Cleveland Road, Cape Ferguson, Townsville, Queensland, 4810, Australia

TYPE OF ORGANIZATION

[X] UNIVERSITY OR OTHER INSTITUTION OF HIGHER EDUCATION
[ ] TAX EXEMPT UNDER INTERNAL REVENUE SERVICE CODE (26 USC 501(a) and 501(c)(3))
[ ] NONPROFIT SCIENTIFIC OR EDUCATIONAL UNDER STATUTE OF STATE OF THE UNITED STATES OF AMERICA
(NAME OF STATE)
(CITATION OF STATUTE)
[ ] WOULD QUALIFY AS TAX EXEMPT UNDER INTERNAL REVENUE SERVICE CODE (26 USC 501(a) and 501(c)(3)) IF LOCATED IN THE UNITED STATES OF AMERICA
[ ] WOULD QUALIFY AS NONPROFIT SCIENTIFIC OR EDUCATIONAL UNDER STATUTE OF STATE OF THE UNITED STATES OF AMERICA IF LOCATED IN THE UNITED STATES OF AMERICA
(NAME OF STATE)
(CITATION OF STATUTE)

I hereby declare that the nonprofit organization identified above qualifies as a nonprofit organization as defined in 37 CFR 1.9(e) for purposes of paying reduced fees under section 41(a) and (b) of Title 35, United States Code with regard to the invention entitled Same as above by inventor(s) Razi VAGO described in

[ ] the specification filed herewith
[X] application serial no. , filed
[ ] patent no. , issued .

I hereby declare that rights under contract or law have been conveyed to and remain with the nonprofit organization with regard to the above identified invention.

If the rights held by the nonprofit organization are not exclusive, each individual, concern or organization having rights to the invention is listed below* and no rights to the invention are held by any person, other than the inventor, who could not qualify as a small business concern under 37 CFR 1.9(d) or by any concern which would not qualify as a small business concern under 37 CFR 1.9(d) or a nonprofit organization under 37 CFR 1.9(e). *NOTE: Separate verified statements are required from each named person, concern or organization having rights to the invention averring to their status as small entities. (37 CFR 1.27)

NAME
ADDRESS
[ ] INDIVIDUAL [ ] SMALL BUSINESS CONCERN [ ] NONPROFIT ORGANIZATION

NAME
ADDRESS
[ ] INDIVIDUAL [ ] SMALL BUSINESS CONCERN [ ] NONPROFIT ORGANIZATION

I acknowledge the duty to file, in this application or patent, notification of any change in status resulting in loss of entitlement to small entity status prior to paying, or at the time of paying, the earliest of the issue fee or any maintenance fee due after the date on which status as a small entity is no longer appropriate. (37 CFR 1.28(b))

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

NAME OF PERSON SIGNING X Peter Isdale
TITLE IN ORGANIZATION X Executive
ADDRESS OF PERSON SIGNING Cape Cleveland Road, Cape Ferguson, Townsville, Queensland, 4810, Australia
Signature: X
DATE X 20/2/2000

"SHAPED PRODUCTS OR STRUCTURES FOR MEDICAL OR RELATED PURPOSES"

FIELD OF THE INVENTION

This invention relates to shaped products or structures, including prosthetic or implant devices, for medical or related purposes, and in particular to prosthetic or implant devices and other shaped products or structures for use in bone tissue engineering in the fields of human medicine and dentistry, as well as in non-human veterinary fields.

BACKGROUND OF THE INVENTION

Crane *et al.* (1995) point out that skeletal deficiencies resulting from trauma, tumours or abnormal development frequently require surgical intervention to restore normal tissue function. Even though current surgical treatments are often successful, all have associated problems with limitations. The limited supply of autograft tissue and the potential of pathogen transfer with allografts have inspired surgeons and engineers to search for other methods to repair skeletal defects. Synthetic materials such as metals and bone cements have also been used for many years, but often result in stress-shielding to the surrounding bone and fatigue failure of the implant.

These authors also point out that recent strategies to engineer bone have focused on the use of natural or synthetic materials as scaffolds for cell transplantation or as conduits to guide new bone growth. The success of the strategy is highly

dependent on the properties of the material, requiring minimally that it be biocompatible, osteoconductive, easily sterilized and degradable over an appropriate time-scale into products that can be metabolized or excreted. In addition, scaffolds for cell transplantation must have a high porosity for maximal cell loading, surface characteristics that support cell growth and differentiated function and appropriate pore morphology for bone tissue ingrowth *in vivo*. The success of conduits relies on their ability to induce surrounding tissue to invade, grow and replace the implanted material.

A variety of materials are under consideration for use as scaffolds or conduits in accordance with these strategies, however there remains a need for new biomaterial that will interact with living bone tissue and modulate bone formation and repair.

In US Patent No. 3,929,971 (Research Corporation) there is disclosed a synthetic biomaterial having a microstructure substantially corresponding to the microstructure of porous carbonate skeletal material of marine life and made up of hydroxyapatite or whitlockite. This synthetic material is made by converting porous carbonate skeletal material of marine life into a phosphate skeletal material possessing a microstructure substantially the same as or corresponding to the microstructure of the carbonate skeletal source material by subjecting the carbonate skeletal material to hydrothermal chemical exchange with a phosphate.

US Patent No. 4,861,733 (Interpore International) discloses calcium phosphate materials useful as bone substitution material or for the manufacture of prosthetic devices which have been prepared from calcium hydroxyapatite material which has a uniformly permeable microporous structure characterised by a substantially uniform pore volume in the range from about 10 to about 90% and by a pronounced three-dimensional fenestrate structure corresponding to the microstructure of the porous carbonate echinoderm or scleractinian coral skeletal material of marine life, by reacting the calcium hydroxyapatite material which has a calcium to phosphorous atomic ratio of about 1.66 with a phosphate-contributing or phosphorous-contributing moiety or with

a calcium-contributing or calcium oxide-contributing moiety so as to alter the calcium to phosphorous Ca/P atomic ratio to yield a calcium phosphate material retaining the above-described microstructure of the porous carbonate echinoderm or scleractinian coral skeletal material but having a calcium to phosphorous Ca/P atomic ratio less than or greater than 1.6.

Related US Patent No. 4,976,736 (Interpore International) discloses synthetic biomaterials useful for onthopedicaneal dental applications which have a base portion of calcium carbonate and a surface layer of a synthetic phosphate such as hydroxyapatite. The base portion may be a calcium carbonate structure having three-dimensional interconnected porosity such as may be found in porous skeletal carbonate of marine life, e.g. coral porites skeletal aragonite, or it may be porous or non-porous granules of calcium carbonate.

SUMMARY OF THE INVENTION

According to one aspect of the present invention, there is provided a shaped product or structure for medical or related purposes, characterised in that it is formed from coral, preferably coral of the species *Porites* or *Acropora* species, particularly *Acropora* species such as *Acropora grandis*.

In this aspect, the present invention also provides a device for medical or related purposes which comprises an assembly of shaped products or structures, as broadly described above.

According to another aspect of invention, there is provided a prosthetic or implant device for medical or related purposes, particularly for use in repair of fracture of a long bone or when elongation of a long bone is required. The prosthetic or implant device of this aspect of the invention comprises an assembly of shaped members formed from coral, preferably coral of the species *Porites* or *Acropora*, the assembly

comprising first and second elongate members each of which is adapted to be fixed at one end to a long bone, the other ends of each of said first and second elongate members being externally and internally threaded, respectively, so that said first member is received by said second member in a threaded inter-engagement to enable the overall length of the device to be adjusted.

The threaded inter-engagement of the first and second elongate members of the device of this invention enables the overall length of the device to be adjusted to the length required for the particular use, that is in repair of a fracture or in elongation of a long bone, before the device is fixed in place, for example between the ends of a fractured long bone.

Preferably, an internally-threaded third member is also provided in threaded engagement with the first member to act as a locking nut and lock the second member with respect to the first member at a desired overall length.

Throughout this specification, unless the context requires, the word "comprise" or variations such as "comprises" or "comprising" will be understood to imply the inclusion of a stated integer or group of integers but not the exclusion of any other integer or group of integers.

DETAILED DESCRIPTION OF THE INVENTION

Coral is the hard deposit consisting principally of calcium carbonate which is built up by minute colonial marine invertebrate animals called coral polyps . The corals of the order *Hydrocoralline* of the Class *Hydrozoa* exist as sessile colonies with a massive encrusting or branching exoskeleton with pits in the surface from which the polyps arise.

The corals of the orders *Alcyonaria* and *Zoantharia* of the Class Anthozoa (Actinozoa) are of different form and habits. Those of the alcyonarians are made up of minute spicules formed within the tissues, occasionally compacted in a hard central rod running through the entire colony and sometimes supplemented by an external covering. Zoantharian corals build up hard deposits externally beneath the basal disk which attaches them to the ocean floor. As new individuals arise from the edge of the living tissue their deposits become continuous with those already laid down and so large colonies produce extensive masses of coral rock. The form of these deposits varies. Some are slender and branching and others rounded and massive. They have received common names such as staghorn coral and brain coral (Van Nostrand's Scientific Encyclopaedia, Eight Edition, Van Nostrand, Reinhold, 1995).

Surgical repair of large cortical and other defects, in both humans and non-humans, resulting from traumas or tumour resection presents many challenges. Significant morbidity is associated with autograft harvest sites and the quantity of material available for use in the repair is limited. A bone defect might regenerate more efficiently if a stromal substitute is implanted to provide a framework for organisation of the osteons. By providing a scaffold containing spaces morphologically compatible with osteons and their vascular interconnections, an association between biocomponents and biologic regenerative and repair responses can be promoted.

Each year, a large number of cases involved with bone fractures and deficiencies result in mechanical fixation using temporary or permanent hardware. The use of natural and biodegradable materials for surgical applications can provide strong, biocompatible and degradable hardware that can be manufactured with low cost and may consequently reduce the need for a second surgical intervention following the healing process. It also can be custom fabricated according to special needs. High risk, elderly patients may represent a particular challenge since increasing the need of a second surgical intervention and hospitalization time is crucial. There is a growing

search for biocompatible and biodegradable materials for use as hardware for surgical applications.

A wide range of metallic, ceramic, polymeric and composite materials have been used in the construction of medical devices for implantation into the human body (Hench and Wilson, 1993). The types of implant can be presented as follows: (1) nearly inert; (2) porous; (3) bioactive; (4) resorbable. Porous structure devices were developed to prevent loosening of the implants. When the porous implant is metal, the large interfacial area can provide a focus for corrosion of the implant and loss of metal ions into the tissue. A film of hydroxyapatite (HA) often coats these, for a more rapid bond of the natural bone to the devices (Hench and Wilson, 1993; Lacefield, 1993; Dunn and Maxiian, 1994). The coatings, however, often dissolve with time, which limits their effectiveness. In porous implants, it is necessary for the pores to be at least 100 micrometers in diameter to allow capillaries to provide a blood supply to the ingrown connective tissue. It is important to note that interfacial stability is crucial for a clinical successful implantation. Resorbable implants are designed to gradually degrade and be replaced with natural tissue, leading to regeneration of tissue instead of its replacement. The difficulty is to meet the requirements of strength and short-term and mechanical performance during the processes.

Carbonate skeletons of coral polyp and other reef-building organisms possess a unique microporous lattice structure. This lattice structure promotes ingrowth of connective tissue and eventual bone deposition within the scaffold. Each species of organism governs the microstructural properties of its skeleton to a high degree, however the morphological parameters used to describe the colonies taxonomically do not suffice to characterise them from a materials standpoint. The rationale for using the calcium carbonate structure of coral as a bone substitute material is based on the fact that natural bone is approximately 70% hydroxyapatite by weight and 50% by volume. Porosity and interconnectivity are key factors with respect to the amount and type of ingrowth of tissue into the lattice structure of coral. For example, in highly

porous and interconnected implants, tissue ingrowth starts by day three or four. By four weeks, the ingrowth is completed and apposition of bone covering the pore walls has began. In animal models, bone ingrowth may be nearly complete by three months.

The study of coral as an osseous substitute began as early as 1970s in France and USA. It reflects different ideas and approaches, the first human graft was carried out in 1979 (Patel *et al.*, 1980). One of the early approaches by American researchers was to replicate the porous calcium carbonate skeletal structure of some marine organisms (White *et al.*, 1972). They replicated the microstructure in ceramic, metal, and polymer prosthetic materials in a process that they termed replamineform (White *et al.*, 1972). In another process, using hydrothermal exchange, coral skeletal carbonate was converted to calcium phosphate (Roy and Linnehan, 1974). The result was a compound with good biocompatibility and hardness, its derivatives are still a common material in bone grafting. There is however a continuous debate (Holmes, 1979; Shors and Holmes, 1993; Marchac and Sandor, 1994; Ripamonti, 1996), over the properties of the converted material. It is argued that the conversion process may cause the coral to lose some of its unique properties that are characterised by its architectural configuration and integration into bone tissue. Both natural and converted coral have undergone some clinical trails and are currently available. Coralline and coralline derivative implants are also under experimental study using animal models (e.g. Glass, 1989; Brain *et al.*, 1993; Ripamonti, 1996) and human clinical trials and evaluation for repair or replacement of broken or diseased bones. Studies are currently being conducted for restoration or replacement of both broken and diseased bone for orthopaedic, cranial, maxillofacial, dental and ocular and orbital floor implants (e.g. Holmes, 1993; Papacharalambous, 1993; Bronzino, 1995; Mercier *et al.*, 1996).

It has also been suggested that in some cases of mechanical failure of internal fixation for hip fractures, which is common in elderly patients, replacement of lost bone trabeculae may improve the mechanical strength of fixation (Cirotteau, 1993). Holmes

(1993) has summarised the main clinical applications for porous hydroxyapatite of marine origin. In most of these cases, solid blocks, rods or granular forms of coralline materials have been used to fill gap and contour defects (Marchac and Sandor, 1994).

It has been noted that the main obstacle in the use of hydroxyapatite and porous coralline materials for load-bearing implants is the relatively poor mechanical properties of these materials, mainly low elasticity and high brittleness, and suggested that future development should focus on the optimisation of properties and microstructural components of the material and impregnation with molecular and cellular agents (Holmes, 1993; Crane *et al.*, 1995; Ashby *et al.*, 1996; Dee and Bizios, 1996).

Particularly preferred for use in the present invention are two species of corals. The first one, *Porites* is more porous and softer; while the other *Acropora* is stronger, harder and less porous.

I. ***Porites***

The entire skeleton deposited by a single polyp or by a colony is the corallum. The skeletons around an individual polyp are corallites and the upper open or end of a carollities is the calyx. The calices are mostly arranged in a hexagonal closed packed array. *Porites* species traditionally have been difficult to distinguish. Confusion results from the fact that some coral species tend to be plastic mainly in response to some environmental parameters such as light intensity, water motion, temperature etc. The plasticity is evidenced by the same species exhibiting a variety of growth forms and colours etc. In most species, the void to solid ratios is generally in the range of 0.4 to 0.6, and the void phase completely interconnects, forming a highly regular network that interpenetrates the solid calcium carbonate phase. In some species, the micro architecture of the solid and void spaces is nearly identical. The species control regulatory of microstructure characteristics is attractive to material scientists because

this uniform and interconnecting architecture has not been matched in man-made, synthetic materials.

Some typical mechanical properties of *Porites* coral

Property	Test	Orientation	Mean	Range
Crush Strength (psi)	Compression	Parallel Perpendicular	1343 626	997-1675 257-963
Ultimate strength ($N\text{-}cm^{-1}$)	Compression	Perpendicular	373	251-544
Stiffness ($N\text{-}cm^{-1}$)	Compression	Perpendicular	8300	3310-11470
Energy absorption (N-cm)	Compression	Perpendicular	9.9	4.5-13
Tensile strength ($gm\text{-}cm^{-2} \times 10^4$)	4-point bending	Not reported	Not reported	2.4-3.3
Young's modulus ($gm\text{-}cm^{-2} \times 10^4$)	4-point bending	Not reported	Not reported	5.2-6.0
Elastic modulus (dynes - $cm^{-2} \times 19^{10}$)	Resonance frequency	Parallel Perpendicular	4.8 2.6	3.6 - 5.8 1.9 - 3.2

Some *Porites* species are highly porous and possess a regular and uniform micro configuration (structure) of the skeleton. Colonies can grow to 10m in diameter and can be found in the reef slopes and lagoons. The average density for *Porites* species from the Great Barrier Reef in Australia is ~1.4 g/cm^3. The average pore size in species growing at outer edge of the Great Barrier Reef is ~200μ but it can vary between the locations.

II. *Acropora*

Acropora species grow widely throughout the tropic seas. The most common growth form of *Acropora* is the branched form with *Acropora grandis* forming staghorn-

like colonies. Branches of a typical colony can be very long (a few metres in height) and as thick as 10-15cm. This species grows 20-25cm a year. Since this species is very common and fast growing, samples can be easily collected in sheltered areas of the coral reefs. In addition it is also very easy to culture this species so that collection from the coral reefs can be avoided by use of cultured coral material.

The average skeletal density of *Acropora grandis* is ~2.7g/cm^3. Because the skeleton of this coral species is dense and strong, it can be easily machined to a variety of configurations of shaped products or structures of different sizes, for example by grinding. This material is particularly suited for use in an implant device, in particular for load bearing bones where strength is an essential property of the implant device.

As previously described, the prosthetic or implant devices and other shaped products or structures of the present invention are provided for medical or related purposes. The term "medical or related purposes" is used throughout this specification to include the fields of human and non-human medicine and dentistry in particular. Thus the shaped products or structures of this invention may be used as bone implants or protheses, or as dental implants or prostheses. In other embodiments, the shaped products or structures may be "hardware" items for medical or related purposes including, but not limited to, various cylinders, sleeves, pins, screws, bolts, nuts, spacers, flat or curved plates or the like. Some typical hardware items are shown by way of example only in Figure 1. These shaped products or structures which are "hardware" items are preferably formed from coral of the species *Acropora*.

The present invention also extends to devices for medical or related purposes which comprise an assembly of two or more shaped products or structures of this invention. Figure 2 shows a typical such device, however it is to be understood that this Figure is included by way of example only and the present invention is not restricted to devices of the type shown in Figure 2.

Figure 2 shows an implant device 10 for insertion between the ends 30 and 31 of a long bone (see Fig 2e), for example the ends formed by fracture of the long bone, or when elongation of the bone is needed. Device 10 comprises a threaded male pin 11 (see Fig 2a), an internally threaded female socket 12 (see Fig 2b) and an internally threaded locking nut 13 (see Fig 2c). Fig 2d shows the assembled device 10. As shown in Fig 2a, male pin 11 (which is optionally hollow as shown at 23) consists of an externally threaded shank portion 21 and a head portion 22 which incorporates a socket 24 of suitable dimensions to receive the end of a long bone, which in use of the device will be fixed into the socket, for example using bone cement or similar material or by use of suitable screws, pins or the like. Female socket 12 is internally threaded as shown at 25, and is similarly provided with a socket 26 to receive the end portion of a long bone. Locking nut 13 is also internally threaded as shown at 27. It will be evident from Fig 2d which shows the assembled device 10 that the overall length of the device, and hence the distance between the ends of a long bone into which the device is inserted, can be adjusted by screwing the female socket 12 along the shank portion 21 of the male pin 11, and then locking the socket 12 in place with the locking nut 13. The various shaped members of the device 10 are preferably formed from coral of the species *Porites* or *Acropora*.

In work leading to the present invention, off-shore coral colonies were collected from the Great Barrier Reef in Australia using lifting bags and baskets. The colonies were immediately soaked in a bleaching solution. Since clearing the residual organic matrix is one of the first tasks in the purification process, the first steps were started immediately following collection of the coral. It has been found that by bleaching the colonies immediately after collection and while the colonies were still wet, the best results and cleanest colonies were obtained.

The colonies were then cut into blocks and machined into a variety of configurations as shown by way of example in Figure 1. After the initial bleaching and cleaning processes, samples were oven dried and kept in a semi-sterile, dry

environment to avoid humidity and bacterial infections of the cleaned skeletal materials.

Special holders were fabricated from soft polyvinyl chloride polymer material to firmly secure the samples to avoid fractures during the machine processing of the samples.

Oven dried samples were transferred into an hydrostatic pressure chamber where distilled water was pressurised (150psi) into the skeleton, and particularly the fine cavities. This process reduces the amount of dust particles produced and allows easier machining (eg. grinding) of the samples. As an alternative, it has been found that dipping samples in liquid nitrogen creates a more solid substrate. After dipping in liquid nitrogen for 2 minutes, processing of the samples was easier and the surface produced by the machine processing was smoother.

As noted above, the products or structures may be machined into a variety of configurations for various medical or related purposes, and quite complex shapes such as cylindrical structures and threaded structures may be formed by appropriate machine processing.

Finally, the shaped products or structures of the present invention may be used to adsorb or bind, and deliver, other therapeutically active substances which assist in the bone repair or regeneration process, or which have other desired therapeutic activity. Such substances include, by way of example, known synthetic or semisynthetic antibiotics which may be introduced into the pore cavities of the shaped product or structure, or a growth factor such as transforming growth factor or one of the bone morphogenic proteins which can be used to assist or promote bone ingrowth.

Persons skilled in this art will appreciate that variations and modifications may be made to the invention as broadly described herein, other than those specifically

described without departing from the spirit and scope of the invention. It is to be understood that this invention extends to include all such variations and modifications.

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CLAIMS:

1. A shaped product or structure for medical or related purposes, characterised in that it is formed from coral.

2. A product or structure according to claim 1, characterised in that the coral is of the species *Porites.*

3. A product or structure according to claim 1, characterised in that the coral is of the species *Acropora.*

4. A product or structure according to claim 3, characterised in that the coral is *Acropora grandis.*

5. A product or structure according to claim 1 which is a hardware item for medical or related purposes.

6. A product or structure according to claim 5, which is a cylinder, sleeve, pin, screw, bolt, nut, spacer, or flat or curved plate, for medical or related purposes.

7. A product or structure according to claim 1, which is a prosthetic or implant device.

8. A product or structure according to claim 1, wherein a therapeutically active substance is adsorbed or bound onto the coral.

9. A product or structure according to claim 8, wherein the therapeutically active substance is an antibiotic.

10. A product or structure according to claim 8, wherein the therapeutically active substance is a growth factor to assist or promote bone ingrowth.

11. A device for medical or related purposes which comprises an assembly of shaped products or structures according to any of claims 1 to 10.

12. A device according to claim 8 which is an assembly comprising first and second elongate members each of which is adapted to be fixed at one end to a long bone, the other ends of each of said first and second elongate members being externally and internally threaded, respectively, so that said first member is received by said second member in a threaded inter-engagement to enable the overall length of the device to be adjusted, and optionally an internally-threaded third member in threaded engagement with the first member to act as a locking nut and lock the second member with respect to the first member at a desired overall length.

ABSTRACT OF THE DISCLOSURE

A shaped product or structure, including a prosthetic or implant device, for medical or related purposes is characterised in that it is formed from coral.

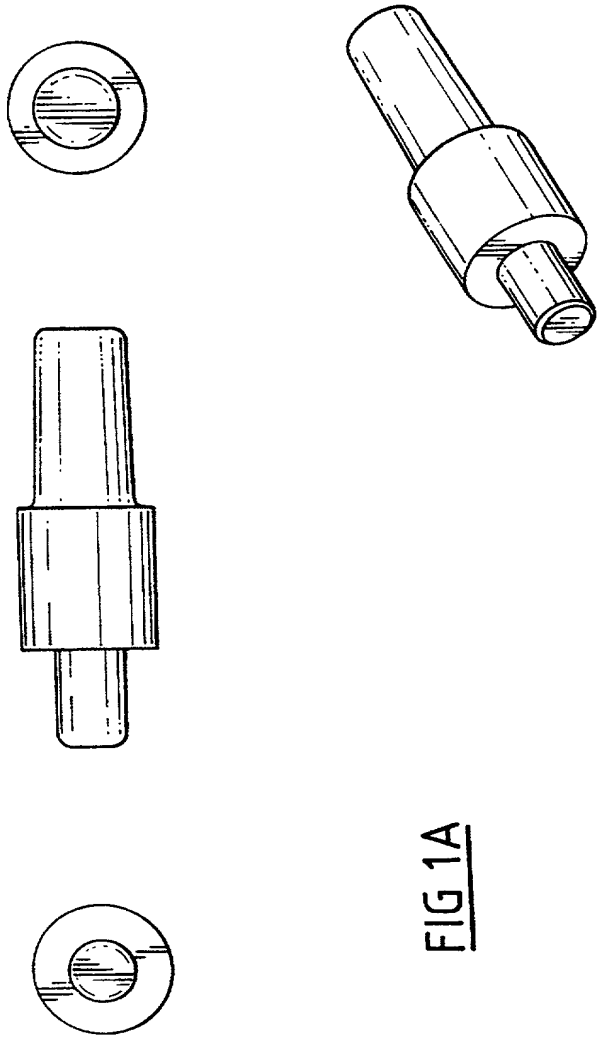
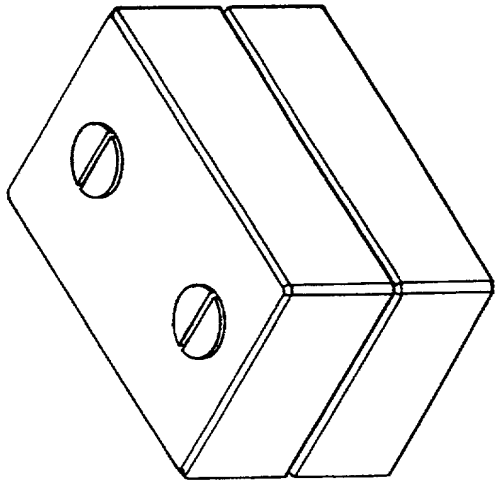


FIG 1A



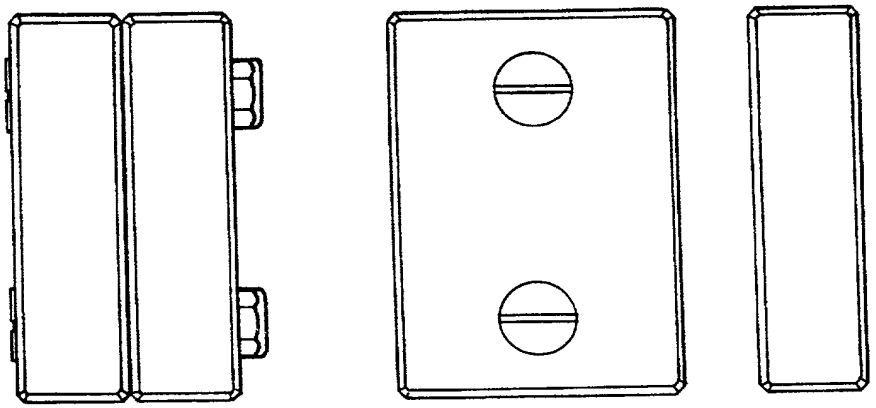


FIG 1B

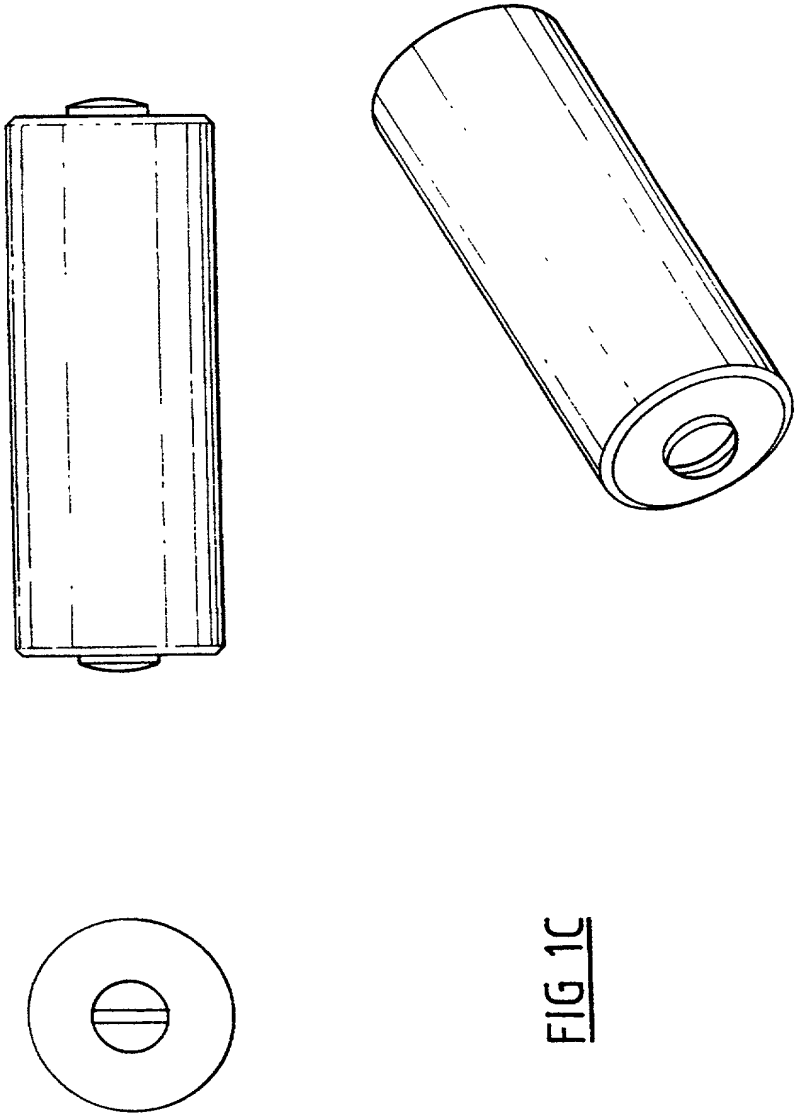


FIG 1C

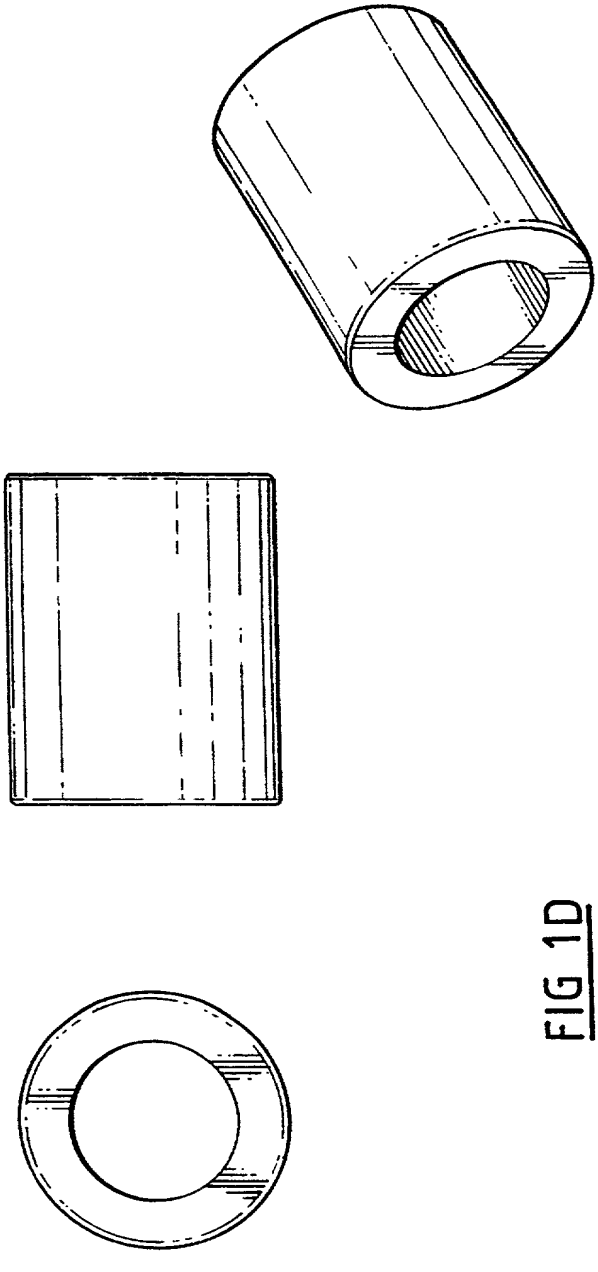


FIG 1D

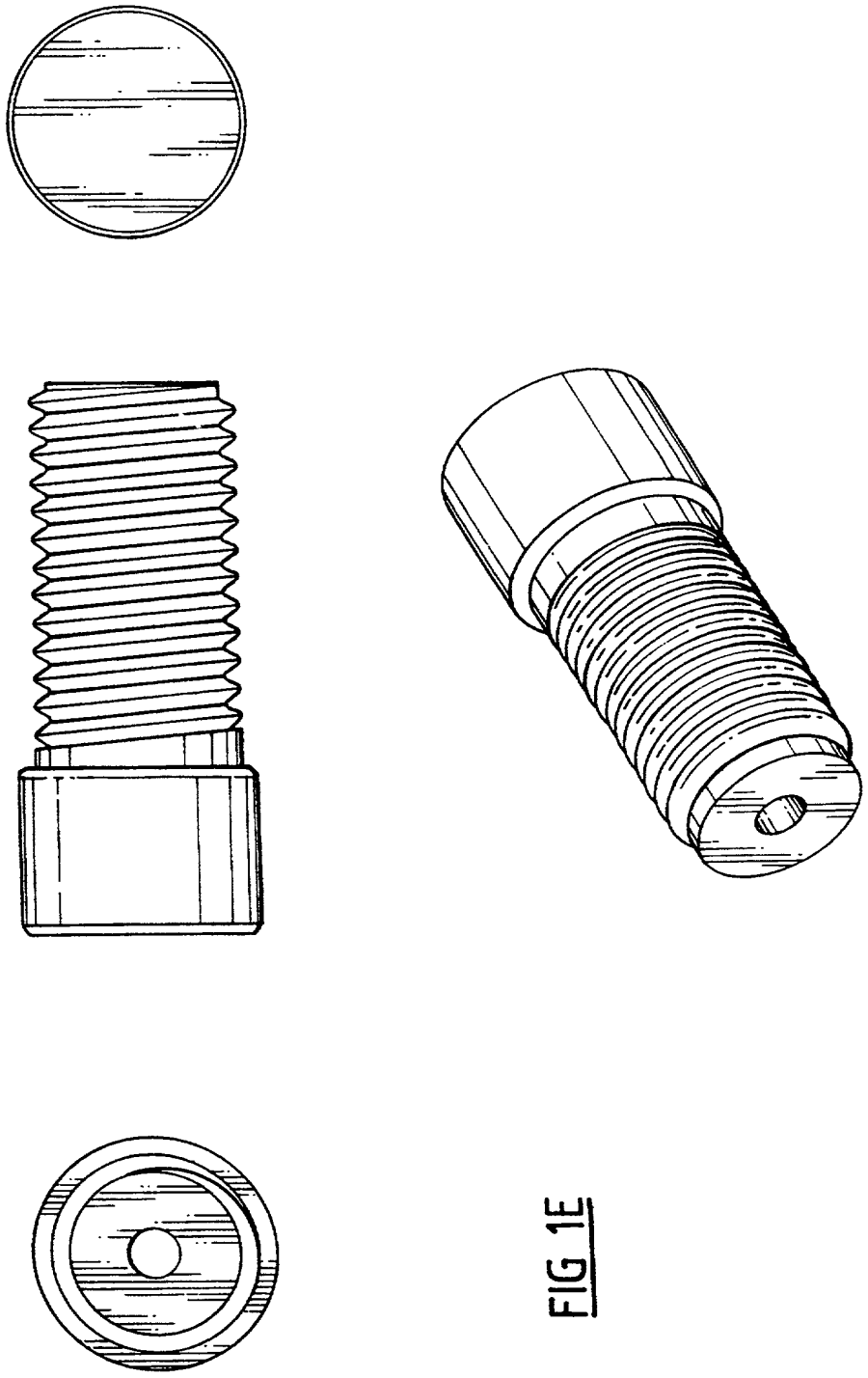
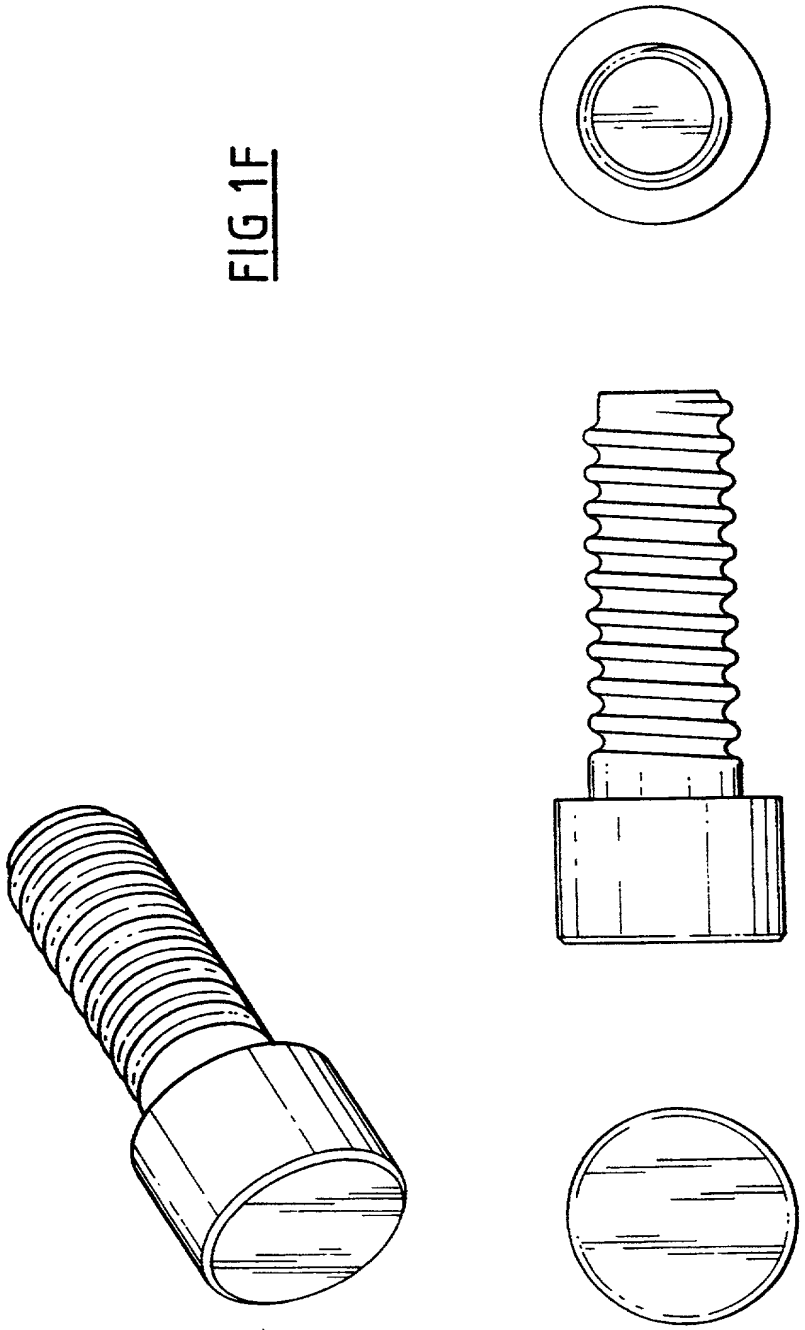


FIG 1E

FIG 1F



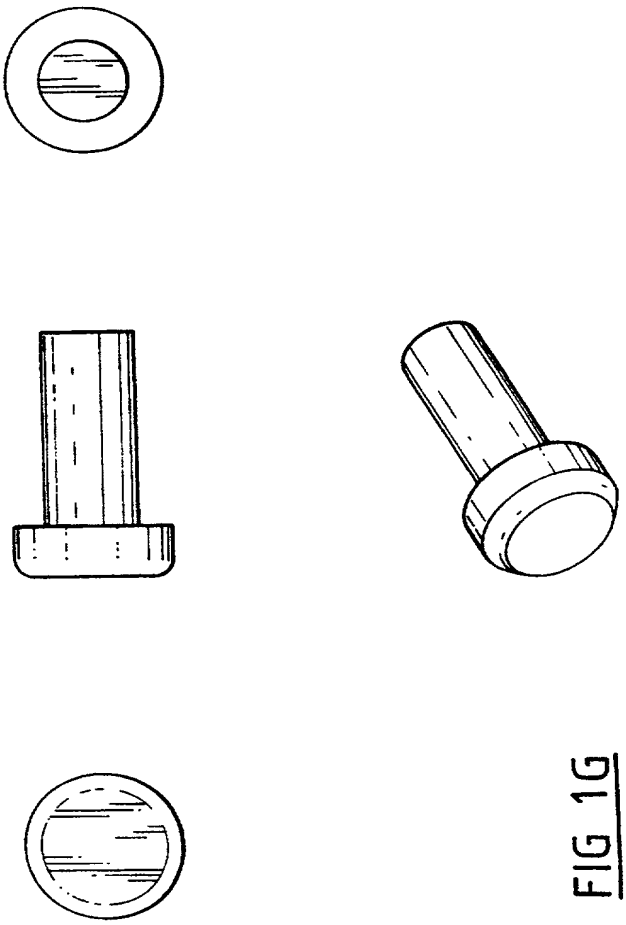


FIG 1G

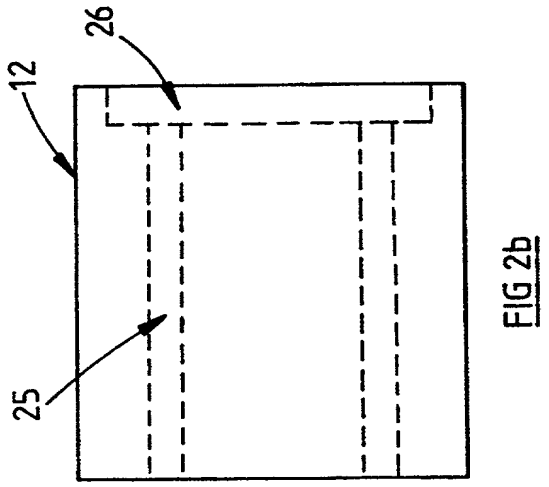


FIG 2b

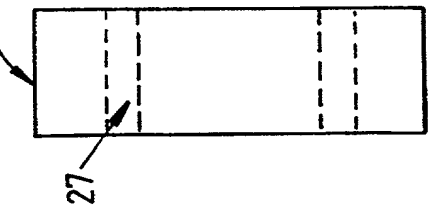


FIG 2c

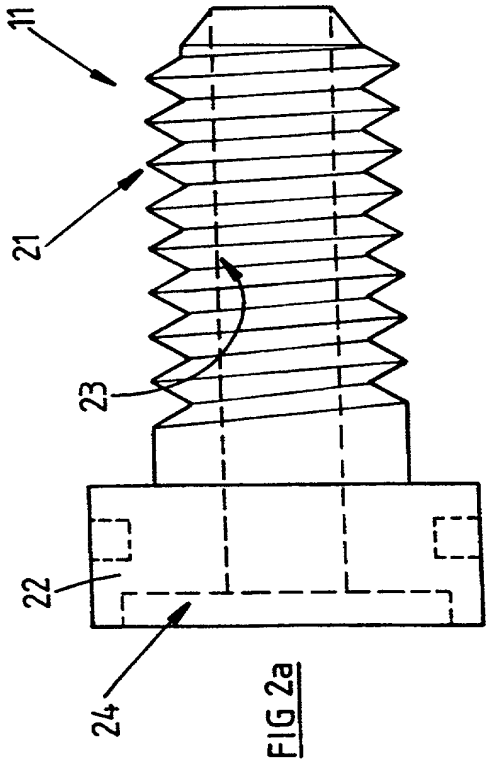


FIG 2a

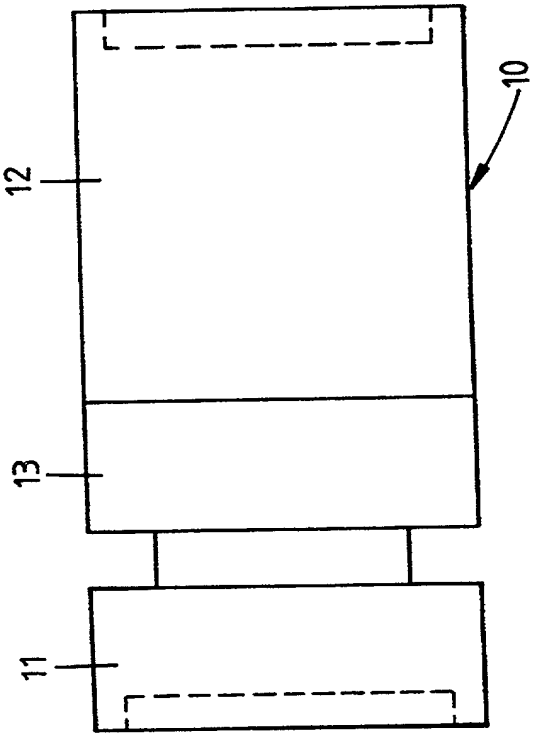


FIG 2d

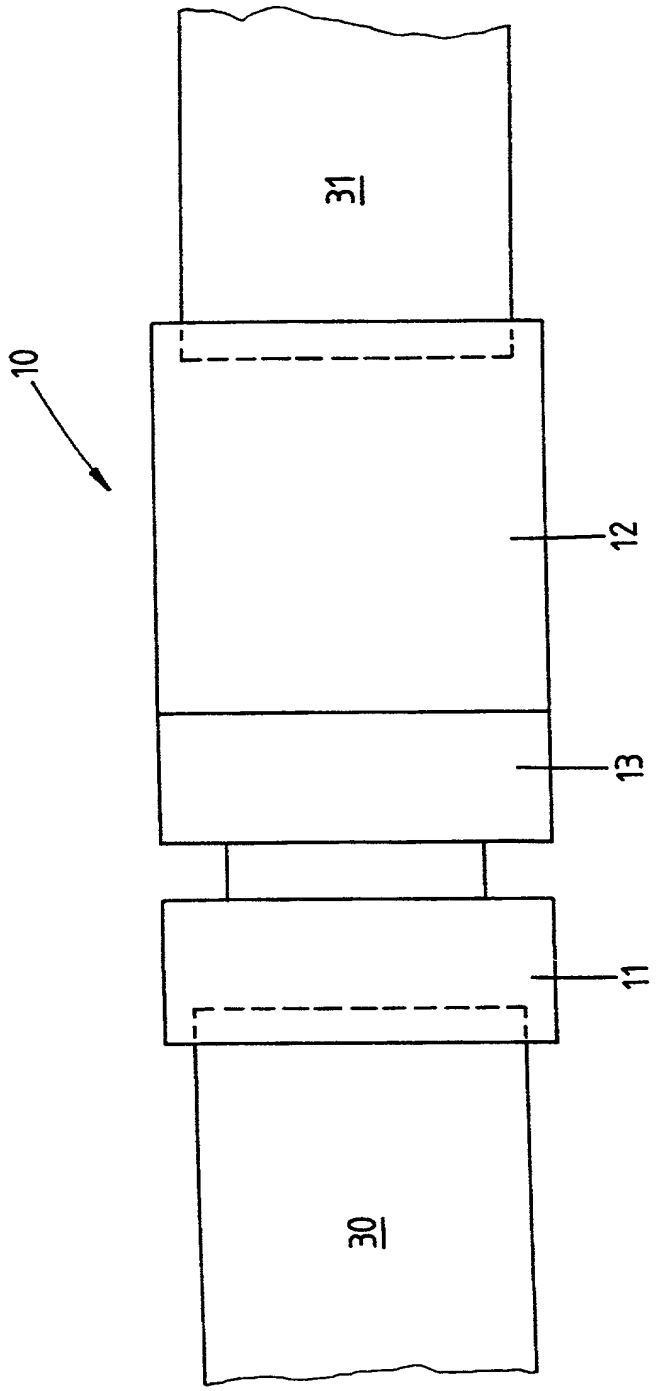


FIG 2e

COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY

(Includes Reference to PCT International Applications)

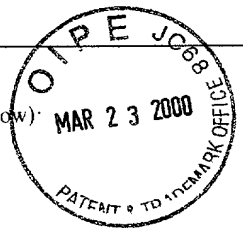
ATTORNEY'S DOCKET NUMBER

As a below named inventor, I hereby declare that

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

"SHAPED PRODUCTS OR STRUCTURES FOR MEDICAL OR RELATED PURPOSES"



the specification of which (check only one item below):

☐ is attached hereto.

☐ was filed as United States application

Serial No. _____

on _____,

and was amended

on _____ (if applicable).

☒ was filed as PCT international application

Number PCT/AU98/00519

on 6 July, 1998,

and was amended under PCT Article 19

on _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowlege the duty to disclose information which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, §1.56(a).

I hereby claim foreign priority benefits under Title 35, United States Code, §119 of any foreign application(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application(s) for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed:

PRIOR FOREIGN/PCT APPLICATION(S) AND ANY PRIORITY CLAIMS UNDER 35 U.S.C. 119:

COUNTRY (if PCT, indicate PCT)	APPLICATION NUMBER	DATE OF FILING (day, month, year)	PRIORITY CLAIMED UNDER 35 USC 119
AUSTRALIA	PO 7705	7 July 1997	☒ YES ☐ NO
AUSTRALIA	PO 7706	7 July 1997	☒ YES ☐ NO
			☐ YES ☐ NO
			☐ YES ☐ NO
			☐ YES ☐ NO

Combined Declaration For Patent Application and Power of Attorney (Continued)
(Includes Reference to PCT International Applications)

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) or PCT international application(s) designating the United States of America that is/are listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in that/those prior application(s) in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowlege the duty to disclose material information as defined in Title 37, Code of Federal Regulations, §1.56(a) which occurred between the filing date of the prior application(s) and the national or PCT international filing date of this application:

PRIOR U.S. APPLICATIONS OR PCT INTERNATIONAL APPLICATIONS DESIGNATING THE U.S. FOR BENEFIT UNDER 35 U.S.C. 120:

U.S APPLICATIONS		STATUS (Check one)		
U S APPLICATION NUMBER	U S FILING DATE	PATENTED	PENDING	ABANDONED

PCT APPLICATIONS DESIGNATING THE U.S					
PCT APPLICATION NO	PCT FILING DATE	U S SERIAL NUMBERS ASSIGNED (if any)			

POWER OF ATTORNEY: As a named inventor, I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith.

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	RESIDENCE & CITIZENSHIP	CITY	STATE OR FOREIGN COUNTRY	COUNTRY OF CITIZENSHIP
	POST OFFICE ADDRESS	POST OFFICE ADDRESS	CITY	STATE & ZIP CODE/COUNTRY
203	FULL NAME OF INVENTOR	FAMILY NAME	FIRST GIVEN NAME	SECOND GIVEN NAME
	RESIDENCE & CITIZENSHIP	CITY	STATE OR FOREIGN COUNTRY	COUNTRY OF CITIZENSHIP
	POST OFFICE ADDRESS	POST OFFICE ADDRESS	CITY	STATE & ZIP CODE COUNTRY

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

SIGNATURE OF INVENTOR 201	SIGNATURE OF INVENTOR 202	SIGNATURE OF INVENTOR 203
X		
DATE: X 22.02.2000	DATE	DATE

[ ] Signature for fourth and subsequent joint inventors.
Number of pages added _____.